# GUIDED MISSILES AGAINST TUMORS

## Using Precision Medicine, Scientists Take Aim at Many Types of Cancer

Chemotherapy is the buckshot of cancer treatment. It's a broad, "one size fits all" approach for most patients. However, each patient's cancer is unique, and major differences exist between patients with the same type of cancer. This limits the effectiveness of chemotherapy. Like buckshot, it can hit the target, but not with optimal accuracy.

Conversely, precision medicines, therapies that target diseases based on attributes like patients' individual genetic mutations, could be the guided missiles of cancer treatment. Yet their accuracy is also a potential limitation: Precision drugs are more specific, but many target only a few types of cancer.

### Testing the Targets

Scientists in the Frederick National Laboratory's Molecular Characterization Laboratory are part of two first-of-their-kind clinical trials striving to overcome this problem. These groundbreaking studies, NCI Molecular Analysis for Therapy Choice (NCI-MATCH) and Pediatric MATCH, seek to make precision medicine more versatile by determining whether drugs that treat one cancer with a certain mutation can treat other types of cancer with the same mutation.

NCI-MATCH is the largest precision medicine trial ever undertaken at NCI, having screened more than 6,000 patients for enrollment since opening. Pediatric MATCH,

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which followed NCI-MATCH, is smaller but equally ambitious. More than 500 children and adolescents with cancer have been screened for enrollment.

## Leadership Advances the Trials

Both trials are testing multiple precision drugs against many cancer types. Regardless of their type of cancer, patients are matched with a drug that has previously shown promise against a mutation detected in their tumors. To do this safely and accurately, clinicians first need to obtain the DNA sequence—the order of genes—of each patient's tumor.

This is where the Molecular Characterization Laboratory has helped. Its staff established and participated in a clinical laboratory network that developed and validated two next-generation sequencing assays, one for each trial. The assays identify the mutations in biopsies taken from the patients' tumors.

During NCI-MATCH's planning stage, the Molecular Characterization Laboratory hosted technicians from the network's partner institutions for one week to teach them the trial's assay and to work alongside them. The training continued after the technicians returned home, soon resulting in an assay with an almost 100 percent sequencing accuracy rate among the laboratories, near-perfect harmony within the network.

"At the time … nobody thought you could get the same [next-generation sequencing] results twice, even in the same laboratory, so it was quite a leap," recalled Mickey Williams, Ph.D., director of the Molecular Characterization Laboratory.

**Mickey Williams, Ph.D.**

Mickey Willians leads the leads the Molecular Characterization Laboratory at the Frederick National Laboratory.

The staff's responsiveness and flexibility have kept operations on track. Both trials aimed for and maintained a two-week turnaround time for the entire biopsy, analysis, and matching process—due in part to the Molecular Characterization Laboratory's support. The staff quickly adapted to obstacles with NCI-MATCH, even redesigning and revalidating the trial's assay to use a new sequencing platform after the original struggled to keep up with an unexpectedly rapid patient enrollment rate.

The Molecular Characterization Laboratory also sequenced 1,250 of the 6,000 biopsies in NCI-MATCH, with three partner institutions sequencing the rest. It continues to sequence biopsies for Pediatric MATCH.

Thanks to ongoing support from the Molecular Characterization Laboratory, both trials can continue to advance precision cancer treatments.

"We're learning a lot about what works and what doesn't, and hopefully these lessons will help guide future studies," Williams said.